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10/564,825	06/16/2006	Pierre-Etienne Chabrier De Lassauniere	58767.000011	3168

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EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/564,825	CHABRIER DE LASSAUNIERE, PIERRE-ETIENNE	
	Examiner	Art Unit	
	VANESSA L. FORD	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-30* is/are pending in the application.

4a) Of the above claim(s) *26-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/2/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of Group I, claims 1-25 filed on September 8, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-10 have been canceled. Claims 26-30 have been added.

Claims 26-30 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on September 8, 2008.

Claims 11-25 are under examination.

Specification Objection

2. The use of the trademark, for example Dysport, page 1 has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. Applicant is asked to review the instant specification for these kinds of informalities and correction is required.

3. It should be noted that the instant specification defines terminal-phase pulmonary distress as having audible breathing problems associated with dying (death rattle). See page 3 of the instant specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 11-23 and 25 are rejected under 35 U.S.C. 103(a) as unpatentable over IN Back et al *(Palliative Medicine 15:329-336)* in view Sanders et al *(U.S. Patent No. 5,766,605 published June 16, 1998)* and further in view of Donovan *(U. S. Patent No. 6,268, 605 published April 9, 2002).*

Independent claim 1 is drawn to a method of treating terminal phase pulmonary distress comprising administering a therapeutically effective quantity of botulinum toxin to a patient suffering from terminal-phase pulmonary distress.

IN Back et a teach that noisy breathing is rattling breathing in dying patients can be great source of distress to relatives, other patients and staff (page 330, 1st column). IN Back et al teach that the noise is usually caused by the retention of secretions from the lung or oropharynx in a patient who is unconscious or too weak to cough or clear them (page 330). IN Back et al teach that these lung secretions are caused by infection or due to heart failure (page 330). IN Back et al teach that almost all of the

patients in the study had a diagnoses of cancer (page 332, 2nd column). IN Back et al teach that the distribution of lung, brain, ear, nose and throat cancer was similar and it is suggested that these form of cancer have a higher incidence of patients that develop death rattle (page 332, 2nd column). IN Back et al teach that treatment usually includes an antimuscarinic drugs as well as repositioning suction, explanation and reassurance for the relatives (page 330, 1st column). IN Back teach that hyoscine hydrobromide is usually the most commonly used antimuscarinic drug to treat death rattle (page 330, 1st column). IN Back et al teach that antimuscarinics such as hyoscine hydrobromide will not remove existing lung secretions (page 335, 1st column).

IN Back et al do not teach botulinum toxin.

Sanders et al teach that botulinum toxin can act upon the autonomic nerve function and can be used to control disorders such as excessive salivation, asthma and chronic obstructive pulmonary disease (COPD) (see the Abstract). Sanders et al teach that botulinum toxin relaxes that bronchial muscles (column 2).

Donovan teaches methods for treating cancer with botulinum toxin to improve patient function (see the Title and the Abstract). Donovan teaches that improved patient function includes reduced pain, reduced time spent in bed, increased ambulation, healthier attitude, more varied lifestyle or healing permitted by normal muscle tone (column 13). Donovan teaches that improved patient function is synonymous with improved quality of life (column 10). Donovan teaches that the parotid gland is a part of the innervation of some paraganglionmas (column 2). Donovan teaches that botulinum toxin inhibits the release of neurotransmitters acetylcholine, dopamine, norepinephrine,

CGRP and glutamate (columns 5-6). Donovan teaches that the botulinum toxin used in the invention is one of the serotypes A-G (column 5). Donovan teaches that botulinum toxins can be stored in lyophilized or vacuum-dried form (column 14). Donovan teaches that botulinum toxin can be reconstituted in water or saline (column 14). Donovan teaches that botulinum toxin can be administered by direct injection (column 9). Donovan teaches that the botulinum toxin (type A) can be administered in an amount of between about 3 U/kg and about 35 U/kg of the patient's weight (column 11). Thus, claim limitations such as therapeutically effective "quantity is a dose of 20 to 2000 LD50 units per type A botulinum toxin per patient", "quantity is a dose of 50 to 1000 LD50 units per type A botulinum toxin per patient", "quantity is a dose of 100 to 500" and "quantity comprises a dose of approximately 250 KD50 units per type A botulinum toxin per patient" is taught by the prior art.

It would be prima facie obvious at the time the invention was made to add botulinum toxin to the composition comprising the antimuscarinic drug, hyoscine hydrobromide in a method of treating terminal phase pulmonary distress because IN Back et al teach that hyoscine hydrobromide is effective at treating death rattle but has no effect alleviating effect on lung secretions, Sanders et al teach that botulinum toxin is effective at treating lung disorders such as excessive salivation, asthma and COPD and Donovan that the administration of botulinum toxin improves overall life functions. It would be expected, absent evidence to the contrary, that the combination of hyoscine hydrobromide and botulinum toxin would be effective at treating patients with cancer and terminal-phase pulmonary distress (e.g. death rattle).

Additionally, *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007), discloses that if a technique has been used to improve one method, and a person of ordinary skill would recognize that it would be used in similar methods in the same way, using the technique is obvious unless its application is beyond that person's skill. *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) also discloses that "The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results". It well known in the art to use hyoscine hydrobromide to treat the death rattle and audible breathing problems but does not alleviate lung secretions. It is known in the art to use botulinum toxin to treat lung/respiratory disorders such as asthma and COPD. See Sanders et al. It is known in the art that botulinum toxin can be used to treat cancer and improve a patient's function. See Donovan. Thus, it would be obvious to apply a known technique to a known product to be used in a known method that is ready for improvement to yield predictable results.

Thus, the combination of prior art references as combined provided a *prima facie* case of obviousness absent convincing evidence to the contrary.

5. Claim 24 is rejected under 35 U.S.C. 103(a) as unpatentable over IN Back et al, Sanders et al and Donovan as applied to claims 11-23 and 25 above and in further view of Ellies et al *(Journal of Oral and Maxillofacial Surgery, Volume, Issue 11, November 2000, pages 1251-1256)(Abstract only).*

Claim 24 is drawn to a method of treating the method of claim 11, wherein said botulinum toxin is injected into the parotid gland or the tensor veli palatini muscle of a patient.

The teachings of IN Back et al, Sanders et al and Donovan have been described previously.

IN Back et al, Sanders et al and Donovan do not teach the claim limitation "wherein said botulinum toxin is injected into the parotid gland of the tensor veli palatini muscle of a patient".

Ellies et al teach a method of administering botulinum toxin into the parotid gland (see the Abstract). Ellies et al teach that the cholinergic pathway of the autonomic nervous system has great importance in the secretion of fluid from the salivary glands, blocking this pathway and local application of botulinum toxin offers a possible therapeutic option for the treatment of hypersalivation in various otolaryngologic and neurologic diseases.

It would be prima facie obvious at the time the invention was made to inject the composition comprising the antimuscarinic drug, hyoscine hydrobromide and botulinum toxin as combined above into the parotid gland in a method of treating terminal phase pulmonary distress because Ellies et al teach that the cholinergic pathway of the autonomic nervous system has great importance in the secretion of fluid from the salivary glands, blocking this pathway and local application of botulinum toxin offers a possible therapeutic option for the treatment of hypersalivation in various otolaryngologic and neurologic diseases.

Additionally, *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007), discloses that if a technique has been used to improve one method, and a person of ordinary skill would recognize that it would be used in similar methods in the same way, using the technique is obvious unless its application is beyond that person's skill. *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) also discloses that "The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results". It well known in the art to use hyoscine hydrobromide to treat the death rattle and audible breathing problems but does not alleviate lung secretions. See IN Back et al. It is well known in the art to use botulinum toxin to treat lung/ respiratory disorders such as asthma and COPD. See Sanders et al. It is known in the art that botulinum toxin can be used to treat cancer and improve a patient's function. See Donovan. It is known in the art that the injection of botulinum toxin in the parotid gland, offers a possible therapeutic option for the treatment of hypersalivation in various otolaryngologic and neurologic diseases. See Ellies et al.

Thus, it would be obvious to apply a known technique to a known product to be used in a known method that is ready for improvement to yield predictable results.

Thus, the combination of prior art references as combined provided a *prima facie* case of obviousness absent convincing evidence to the contrary.

Status of Claims

6. No claims allowed.

Conclusion

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to VANESSA L. FORD whose telephone number is (571)272-0857. The examiner can normally be reached on 9 am- 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on (571) 272-0756. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Vanessa L. Ford/
Examiner, Art Unit 1645
December 8, 2008